# Air Break During Preoxygenation and Risk of Altitude Decompression Sickness

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**Pilmanis AA, Webb JT, Balldin UI, Conkin J, Fischer JR.** ***Air break during preoxygenation and risk of altitude decompression sickness.*** **Aviat Space Environ Med 2010; 81:944–50.**

***Introduction:*** To reduce the risk of decompression sickness (DCS), current USAF U-2 operations require a 1-h preoxygenation (PreOx). An interruption of oxygen breathing with air breathing currently requires significant extension of the PreOx time. The purpose of this study was to evaluate the relationship between air breaks during PreOx and subsequent DCS and venous gas emboli (VGE) incidence, and to determine safe air break limits for operational activities. ***Methods:*** Volunteers performed 30 min of PreOx, followed by either a 10-min, 20-min, or 60-min air break, then completed another 30 min of PreOx, and began a 4-h altitude chamber exposure to 9144 m (30,000 ft). Subjects were monitored for VGE using echocardiography. Altitude exposure was terminated if DCS symptoms developed. Control data (uninterrupted 60-min PreOx) to compare against air break data were taken from the AFRL DCS database. ***Results:*** At 1 h of altitude exposure, DCS rates were significantly higher in all three break in prebreathe (BiP) profiles compared to control (40%, 45%, and 47% vs. 24%). At 2 h, the 20-min and 60-min BiP DCS rates remained higher than control (70% and 69% vs. 52%), but no differences were found at 4 h. No differences in VGE rates were found between the BiP profiles and control. ***Discussion:*** Increased DCS risk in the BiP profiles is likely due to tissue renitrogenation during air breaks not totally compensated for by the remaining PreOx following the air breaks. Air breaks of 10 min or more occurring in the middle of 1 h of PreOx may significantly increase DCS risk during the first 2 h of exposure to 9144 m when compared to uninterrupted PreOx exposures.

**Keywords:** denitrogenation, renitrogenation, venous gas emboli, break in prebreathe.

ALTITUDE DECOMPRESSION sickness (DCS) is caused by gas bubble formation resulting from tissue nitrogen ($N_2$) supersaturation. The pressure of bubbles on vessels, nerves, and other tissues causes an array of symptoms, mostly joint pain, but can also include skin, respiratory, and central nervous system symptoms. Although mild joint pain DCS may not be reported by a busy crewmember, more severe pain can interfere with performance by distraction or limited capability to move. Other more serious symptoms involve the pulmonary system, or the central nervous system, and can also result in performance degradation, incapacitation, and may even be fatal. The long-standing operational response to DCS symptoms is descent and the use of 100% oxygen ($O_2$) breathing before and during flight. With the use of these procedures and with the advent and use of pressurized aircraft cabins since WWII, the incidence of fatal altitude DCS is virtually nonexistent.

The risk of DCS is routinely reduced by breathing 100% $O_2$ (preoxygenation or prebreathing) as a means to remove tissue $N_2$ prior to ascent to altitude. These preoxygenation (PreOx) procedures are used to support high altitude reconnaissance aircraft flights, high altitude airdrop/parachuting, high altitude flights in unpressurized aircraft, hypoxia training in altitude chambers, and extravehicular activity in space. In U-2 operations, 1 h of PreOx is a requirement before commencement of a mission. During such PreOx periods, unavoidable unplanned interruptions in $O_2$ breathing can occur. "Breaks in prebreathe" (BiP) are handled several ways. In some cases, the PreOx period is started over, in some cases the break is ignored, and in some cases an improvised "payback" schedule is used. There are no published data to support these procedures.

Little conclusive data has been published on the effect of an air break during PreOx on DCS incidence. Bateman (4) evaluated long PreOx periods and long air breaks in PreOx, and found that there was little impact on DCS from the air breaks. Clarke et al. (7) showed that a 90 min air break after the PreOx period greatly increased the DCS rate. Cooke (9) addressed this question by evaluating the effects of 5-min and 10-min air breaks on DCS incidence at different times during PreOx. These breaks were tested in a 60-, 120-, and 180-min PreOx followed by exposures to 10,058 m (33,000 ft) for 2 h. The control, which was uninterrupted PreOx, resulted in no reported cases of DCS in 17 subjects. One of the six profiles with an air break resulted in two cases of DCS and the other five profiles with an air break resulted in one case each of DCS. Thus, they found no significant effect of any interruption in PreOx (taken individually or summed together) on DCS incidence. Because of the small sample size, no scientifically sound conclusions could be drawn from these data.

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Barer et al. (5) concluded from their study that a 3-min air break after a 2-h PreOx with exposures to 9296 m (30,500 ft) for 4 h including exercise significantly increased the subsequent incidence of DCS, and that a 10-min BiP was not different from a 3-min BiP. However, the breathing gas varied from 89 to 95% $O_2$. Due to this variability in the results in the literature on the effect of an air break during PreOx on DCS incidence, no definitive conclusions can be drawn.

The purpose of this study was to define the relationship between an air break during a 1-h PreOx and the subsequent DCS and venous gas emboli (VGE) incidence. We hypothesized that a relatively short (10- to 20-min) BiP would not result in a significantly higher incidence of DCS or VGE during a subsequent altitude exposure when compared to a PreOx of equal time without an air break. A relatively short BiP would likely only impact the fast $N_2$-exchange tissues, tissues such as blood that quickly equilibrate to a new partial pressure of $N_2$. The renitrogenation during air breathing would be erased rapidly when $O_2$ breathing was resumed. Further, the denitrogenation process initiated at the start of PreOx would continue in the slower tissues during the short "break." Since most altitude DCS symptoms are caused by bubbles in the slow tissues, there would be no impact on DCS incidence.

Our hypothesis continued that with longer air breaks (60 min), the DCS and VGE incidences would be significantly greater than those in the same exposure without the air break. The hypothesis was that 60 min of breathing air would be sufficient time to completely renitrogenate fast tissues, those that are well-perfused, and to begin renitrogenation of the less well-perfused tissues. This renitrogenation would nullify the partial denitrogenation that we believed would continue during the 10- to 20-min air break exposures. It was our intent that the data from this study might make it possible to determine the maximum acceptable air break in the middle of a 1-h PreOx, might provide a rationale to modify existing compensation tables and procedures, and would therefore benefit all operations requiring PreOx.

## METHODS

### *Subjects*

The voluntary, fully informed consent of the subjects was obtained in accordance with a protocol approved by the USAF Surgeon General's Research Compliance office in accordance with existing regulations. All subjects passed an appropriate physical examination and were representative of the USAF rated aircrew population. They were not allowed to participate in scuba diving, hyperbaric exposures, or flying for at least 48 h before each scheduled altitude exposure. Prior to each altitude exposure, a physician conducted a short physical examination of subjects to identify any signs of illness or other problem that would endanger the subject or bias the experimental results. The subjects received a briefing on the morning of each exposure which emphasized their responsibility to report any DCS symptoms or change in well-being to chamber personnel and a list of symptoms was posted in plain view inside the chamber. Air Force Research Laboratory (AFRL) Medical Monitors insured subject health and safety, and made the diagnosis of DCS.

### *Equipment*

All altitude research exposures were accomplished in an altitude chamber used for scientific research with human subjects at Brooks AFB/City-Base, TX. A neck-seal respirator made by Intertechnique® (Plaisir Cedex, France) was used to deliver the breathing gas. This mask provided a slight (2 cm of water) positive pressure which reduced the opportunity for inboard leaks of air from the atmosphere and was more comfortable than the standard aviator's mask. A Hewlett Packard® SONOS 1000 Doppler/Echo-Imaging System (Andover, MA) was used to monitor for VGE. This system permits both audio and visual monitoring and recording of gas emboli in all four chambers of the heart. VGE were graded on a 0–4 integer modified Spencer Scale (12). For this report, any grade from 1 through 4 was considered to be a VGE event.

### *Procedures*

Chamber ascent and descent rate did not exceed 1524 $m \cdot min^{-1}$ (5000 fpm) to and from 9144 m (30.1 kPa; 4.37 psia; 226 mmHg; 30,000 ft). Subject activity at 9144 m consisted of a 16-min sequence of exercise and VGE monitoring. Moderate activity consisting of upper-body exercises was performed by the subjects followed by 4 min of VGE monitoring. The subjects walked less than 10 steps between exercise stations and the echo-imaging station at 4-min intervals. The moderate exercises simulated EVA activities and each lasted 4 min: A) hand-cranked cycle ergometer (24 rpm; 20 W); B) torque wrench (25 ft-lb or 33.9 Nm with an 18" torque wrench) for 5 s each position); and C) rope pull (pulley with 17 lb or 7.7 kg) of weight lifted. To provide relief from boredom and more closely emulate operational distractions, action-oriented movies were shown to the subjects during the hypobaric exposures and the subjects were not questioned about how they felt during the altitude exposures. Each subject was alone in the chamber while at altitude. The echo imaging transducer was placed using a robotic arm operated from outside the chamber. The subjects were instructed to report any changes in well-being to the Medical Monitor and the determination to terminate the exposure was made from these reports. The subjects were examined after recompression to ground level. The Medical Monitors were trained in the diagnosis of DCS and had the ability to consult with the physicians in Hyperbaric Medicine within the same building. Endpoints of the exposures were: 1) completion of the scheduled exposure period, 2) diagnosis of DCS, or 3) detection of left ventricular gas emboli. A more detailed description of the endpoints can be found elsewhere (10).

Three BiP profiles were tested. The breathing gas during all PreOx and exposure periods was 100% $O_2$. All

PreOx was done at "ground level" (180 m above sea level). During the PreOx period subjects were in a seated position. The three profiles tested were identical except for the duration of the air break occurring during the PreOx period. Subjects were exposed to 30 min of PreOx, followed by either a 10-min (32 men, 8 women), 20-min (34 men, 6 women), or 60-min (29 men, 3 women) air break, and then completed the remaining 30 min of PreOx. The subjects then began a 4-h altitude exposure to 30.1 kPa (4.37 psia). Control data to compare against the three BiP profiles were taken from previous studies documented in our DCS database which used identical altitude and activity while decompressed, but were preceded by an uninterrupted 60-min prebreathe (15). There were two basic control profiles. One control profile (28 men) (13) used an altitude exposure of 4 h and the subjects performed their PreOx in a supine position. In the other control profile (67 men), the altitude exposure lasted only 2 h, and PreOx was performed in a seated position. Although not significant ($P > 0.050$), the seated PreOx did yield 7% more DCS, which may reflect a slight advantage of better venous return with improved tissue perfusion while supine, hence better denitrogenation efficiency. This effect is consistent with the data reported by Balldin (1). In this paper, our goal was to use the maximum amount of available data when comparing the BiP profiles with the controls. Thus, for comparisons during the first 2 h of altitude exposure, all 95 (28 + 67) controls were used and for comparisons involving exposure times greater than 2 h, only the 28 controls exposed for 4 h were used.

*Analysis*

A 2-stage process was employed for statistical comparisons of DCS and VGE (any grade) cumulative incidence between the three BiP profiles, and between the BiP profiles and the control data. First, to obtain an overview of the DCS and VGE distributions, we calculated Kaplan-Meier estimates of the survival functions (accounting for censored observations) for each of the BiP and control profiles. Survival time, in our study, is defined as the elapsed time from the start of the altitude exposure to the first report of a DCS symptom (or VGE event). The survival curves were then compared using the Tarone-Ware log-rank test, with $P = 0.05$ as the significance level. The second stage was to compare the four profiles (three BiP profiles plus control) at critical points in time. Specifically, Pearson's Chi-square tests were used to test for differences in DCS (or VGE) cumulative incidence at 1, 2, and 4 h into the altitude exposure. Since there is no scientific rationale to suggest that BiP will reduce DCS risk, our alternative hypothesis for these tests was that BiP would increase DCS risk compared to controls. Therefore, the significance level was set at $P = 0.05$, 1-tailed. All of the statistical tests reported in this paper require an underlying assumption of independence among the subject groups. This is not strictly the case in our study. The experimental design was not "repeated measures" nor was it strictly "independent" (i.e., using different subjects for each of the four profiles). The design was a mixture of both. For example, only 6 of the 95 subjects who performed a control exposure also performed 1 of the 3 air breaks. Therefore, we considered our 95 controls as independent of the 3 air breaks. There were 15 subjects who performed all 3 air breaks, 16 who performed 2 air breaks, and 18 who performed only 1 air break. So clearly our air break exposures are a mixture of independent and repeated measures. In addition, we did not control for any trial order effect. For practical reasons, given a large number of transient military subjects in a study lasting about 3 yr, those subjects who did repeat exposures performed the 10-min break first, then the 20-min, and finally the 60-min break. We assume that the mixed sample design and any trial order effect had a minimal influence on our conclusions.

## RESULTS

**Table I** shows the anthropometric and physiologic means and standard deviations for the control and BiP test subjects. Note that 2 sets of results are shown for the controls: one for the 28 subjects who participated in the 4-h exposure protocol, and one for the entire group of 95 subjects (28 + 67). The anthropometric and physiologic means for the three BiP profiles are nearly identical, reflecting the fact that many of the same subjects participated in multiple BiP profiles. One-way ANOVAs and post hoc multiple comparison Tukey HSD tests were used to compare the BiP and control means. We found the means to be very similar for the majority of the measures. However, a few differences were detected. Mean percent body fat was significantly lower in all three BiP groups compared to the 4-h controls [ANOVA $F(3,99) = 6.09$, $P = 0.001$; Tukey $P < 0.01$ in each case]. Also, mean age was significantly higher in the 20-min and 60-min BiP groups compared to both control groups [ANOVA $F(3,203) = 4.15$, $P = 0.007$ and $F(93,136) = 4.14$, $P = 0.008$ for comparisons with 2 h and 4 h, respectively; Tukey $P < 0.05$ in each case].

The distributions of the cumulative incidence of DCS are shown in **Fig. 1** for the three BiP profiles and for controls. There are 3 curves presented for controls representing: 28 subjects with 4 h exposure; 67 subjects with 2 h exposure; and the 95 combined subjects covering the first 2 h. From a visual inspection of the figure, it appears that the three BiP curves are similar in shape, and that they differ from the control curves, with the differences occurring chiefly in the early part of the exposure. The Tarone-Ware log-rank tests, when performed on the 4-h curves, did not find differences among the three BiP curves, but the 60-min BiP curve differed significantly from the control curve [$\chi^2(1df) = 3.85$, $P = 0.050$] and the test of the 20-min BiP curve vs. control curve approached significance [$\chi^2(1df) = 3.63$, $P = 0.057$]. The Tarone-Ware tests on the 2-h curves, which tended to be more powerful due to the increased sample size in the control group, again did not detect differences among the three BiP curves. However, the 20-min and 60-min BiP curves were statistically different from the control curve [$\chi^2(1df) = 7.61$, $P = 0.006$ and $\chi^2(1df) = 4.87$, $P = 0.027$,

**TABLE I. ANTHROPOMETRIC AND PHYSIOLOGIC VALUES FOR CONTROLS AND BiP SUBJECTS.**

| | Weight, kg | | Height, cm | | BMI | | Body Fat %† | | $VO_{2peak}$† | | Age, yr | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Group (N) | Mean | SD | Mean | SD | Mean | SD | Mean | SD | Mean | SD | Mean | SD |
| 4-h Controls (28) | 85.0 | 12.0 | 178.0 | 8.0 | 26.7 | 2.6 | 21.6 (18) | 4.4 | 3.1 (27) | 0.7 | 29.2 | 5.4 |
| 2-h Controls (95) | 83.5 | 11.4 | 177.1 | 7.6 | 26.5 | 2.7 | 17.0 (75) | 5.4 | 3.4 (91) | 0.6 | 30.8 | 6.0 |
| 10-min BiP (40) | 79.5 | 12.8 | 175.1 | 9.2 | 25.9 | 2.9 | 15.7* (30) | 7.1 | 3.0 (26) | 0.6 | 32.5 | 6.5 |
| 20-min BiP (40) | 79.1 | 11.6 | 175.4 | 9.4 | 25.7 | 2.7 | 15.1* (27) | 6.5 | 3.0 (18) | 0.6 | 34.2** | 7.5 |
| 60-min BiP (32) | 82.5 | 13.9 | 177.5 | 8.2 | 26.1 | 3.0 | 14.4* (28) | 5.2 | 3.2 (8) | 0.5 | 34.7** | 6.8 |

† Body Fat and $VO_{2peak}$ measurements were not available for all subjects. Numbers in parentheses show the actual sample sizes for these two variables.
* Significantly different from the 4-h control mean ($P < 0.01$, Tukey HSD test).
** Significantly different from the 2-h and 4-h control means ($P < 0.05$, Tukey HSD test).

respectively], and the difference between the 10-min BiP and control curves approached significance [$\chi^2(1df) = 2.99$, $P = 0.084$].

To provide insight into the results found with the Tarone-Ware tests, cumulative DCS rates at specific time points were extracted from the DCS curves for each profile and compared. The Chi-square tests found no significant differences among the three BiP profiles at any time point (*P*-values not shown in the table). However, the DCS rates of all three BiP profiles were significantly higher than the control DCS rate at 1 h into the exposure [$\chi^2(1df) = 3.42$ $P = 0.033$, $\chi^2(1df) = 5.75$ $P = 0.008$, and $\chi^2(1df) = 5.86$ $P = 0.008$ for the 10-min, 20-min, and 60-min BiP profiles, respectively]. At 2 h into the exposure, the 20-min and 60-min profile DCS rates were still significantly higher than the control rate [$\chi^2(1df) = 3.90$, $P = 0.024$ and $\chi^2(1df) = 2.86$, $P = 0.046$, respectively]. At 4 h of exposure, no differences were detected between BiP profiles and control.

Distributions of VGE cumulative incidence are shown in **Fig. 2** for the BiP profiles and controls. Visual inspection shows that, regardless of the profile used, VGE incidence increased fairly rapidly after exposure began. The BiP curves do not appear to differ from each other or from the 2-h control curve. The control curve based on the 4-h exposure subjectively appears to be slightly lower than the other curves. However, the Tarone-Ware tests did not detect significant differences among the BiP curves nor between any BiP curve and either control curve. VGE rates at specific time points were extracted from the curves and are presented in **Table II**. Even though the Tarone-Ware tests were not significant, Chi-square tests were performed to compare profiles and no significant differences were found (test results not shown in the table).

The distributions of the types of DCS symptoms observed in our study are shown in **Table III**. The five categories shown were chosen from previous AFRL and NASA publications (3,2,8,11). Although some headaches may result from other causes, the majority are very likely CNS symptoms. Retrospective clarification is not possible based on available data (6). From the table we see that the most common DCS symptom occurring in all groups was joint pain, representing 53% of all symptoms seen in the control group and ranging from 46 to 61% in the BiP groups. The second most common symptom in all groups was skin manifestations (18% in controls and ranging from 17 to 34% in the BiP groups. The remaining three symptom types occurred relatively infrequently in all groups, with no one symptom exceeding 14% in any group. These results suggest that the relative distribution of symptom types in each of the BiP groups mirrored the distribution seen for the controls.

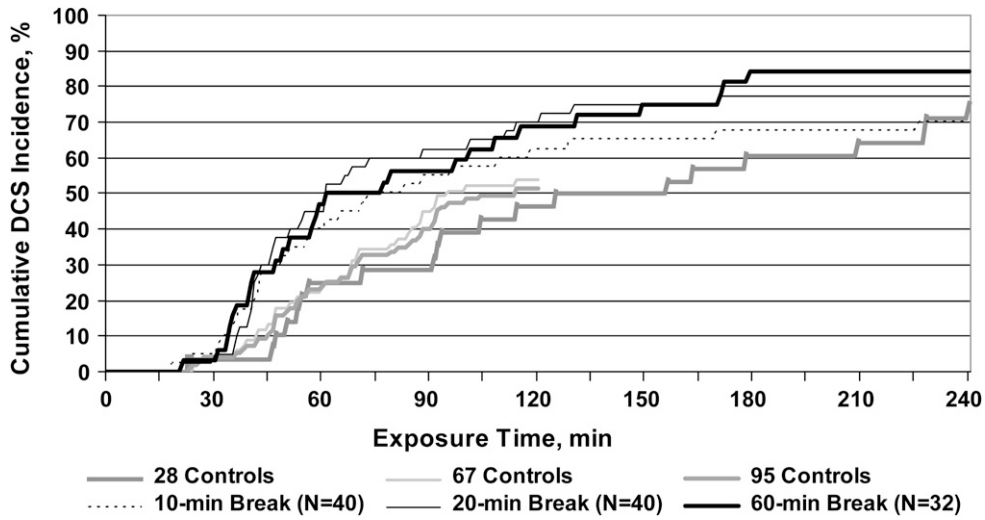


**Fig. 1.** Cumulative % DCS vs. time at altitude for controls and three air break conditions.

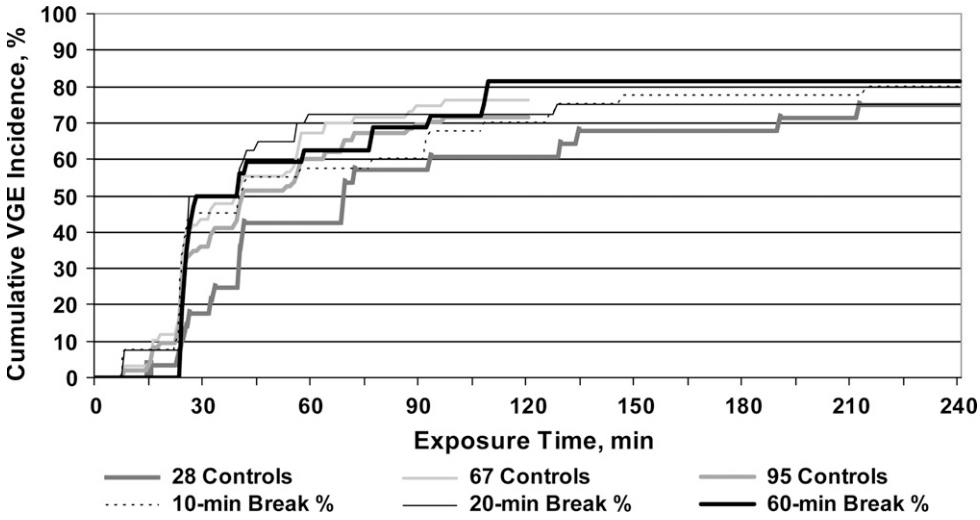


**Fig. 2.** Cumulative % VGE vs. time at altitude for controls and three air break conditions.

## DISCUSSION

Definitive data using current acceptable endpoint criteria for evaluating altitude DCS risk associated with air breathing breaks in PreOx is not available. Direct measurement of denitrogenation/renitrogenation in the tissues of the body is not now technically feasible. Indirect measurement of this process using DCS symptomatology and intravascular bubble detection (VGE) was used in this study. DCS symptoms are subjective, whereas measurement of VGE is objective.

Our results showed that air breaks in PreOx did not change the relative distribution of the types of DCS symptoms compared to controls: joint pain was the predominant symptom in the BiP and control groups; skin manifestations were the second most prevalent in all groups; and occurrence of the remaining symptoms was mixed, but infrequent. On the other hand, the data did show significant differences between the BiP groups and controls with respect to the overall incidence of DCS. Fig. 1 gave a visual impression that the cumulative DCS incidence curves for the BiP groups were different from the control curves and this impression was confirmed by the Tarone-Ware tests. The follow-up tests at specific time points indicated that there was an increased risk of DCS in the BiP groups, compared to control, during the early part of the altitude exposure. At 1 h into the exposure, the cumulative DCS rates of all three BiP groups were significantly higher than that of the controls, and after 2 h of exposure, the 20-min and 60-min BiP rates remained higher than the control rate. We did not find significant VGE incidence differences among the BiP profiles and control at any point during altitude exposure. The VGE incidence rate increased rapidly very early into the exposure in all groups and exceeded 70% in each group by 2 h of exposure.

The fact that the DCS rates of the BiP profiles and controls become similar toward the end of 4 h of altitude exposure is probably due to two factors. First, there is a "ceiling effect." Mathematically, DCS rates cannot exceed 100% (the ultimate ceiling), but since there are some subjects who are naturally resistant to DCS (16), a more likely ceiling is around 75–80%. The BiP DCS rates reach that point early and can go no higher, whereas the control DCS rates rise more gradually, but eventually reach that same ceiling. Second, during the altitude exposure, denitrogenation continues since subjects are breathing 100% $O_2$. It is likely that this additional "denitrogenation period" has been sufficient to reduce $N_2$ in the BiP subjects' slow tissues (such as joints, which have low perfusion) to levels comparable to those in the controls.

Because the DCS rates of the BiP and control subjects were similar toward the end of the 4-h exposures, one might be willing to assume that, for a prolonged operational mission, breaks in PreOx do not matter since the ultimate risks of DCS are the same. The danger with this assumption is that we do not know the incidence rates of serious DCS events (debilitating joint pain, serious neurologic events, etc.). In research studies, once a subject experiences any DCS symptom, the exposure is terminated for the safety of the subject. Consequently, we do not have a clear understanding of how many subjects with mild symptoms might have gone on to develop serious DCS events. However, we surmise that, once an individual develops symptoms, they are likely not to improve, and may worsen. Thus we argue that, in an operational setting

**TABLE II. CUMULATIVE INCIDENCE (%) OF DCS AND VGE AFTER 1, 2, AND 4 h OF EXPOSURE.**

| | 1 h | | 2 h | | 4 h | |
|---|---|---|---|---|---|---|
| | DCS | VGE | DCS | VGE | DCS | VGE |
| **Control (N)** | | | | | | |
| 4 h (28) | | | | | 75% | 75% |
| 2 h (95) | 24% | 60% | 52% | 72% | | |
| **BiP (N)** | | | | | | |
| 10 min (40) | 40% * | 58% | 63% | 70% | 70% | 80% |
| 20 min (40) | 45% * | 73% | 70% * | 73% | 78% | 75% |
| 60 min (32) | 47% * | 63% | 69% * | 81% | 84% | 81% |

* Indicates a significant ($P \leq 0.050$, 1-tailed) difference from Control, based on Pearson's Chi-square test.

**TABLE III. DISTRIBUTION OF THE TYPES OF DCS SYMPTOMS OBSERVED.**

| Profile (N) | Joint Pain | Skin Manifestations* | Respiratory† | CNS‡ | Other§ | Total |
|---|---|---|---|---|---|---|
| Controls (95) | 45 (53%) | 15 (18%) | 9 (11%) | 12 (14%) | 4 (5%) | 85 |
| 10-min BiP (40) | 22 (61%) | 6 (17%) | 3 (8%) | 3 (8%) | 2 (6%) | 36 |
| 20-min BiP (40) | 20 (54%) | 10 (27%) | 2 (5%) | 3 (8%) | 2 (5%) | 37 |
| 60-min BiP (32) | 16 (46%) | 12 (34%) | 5 (14%) | 2 (6%) | 0 (0%) | 35 |
| All BiP (112) | 58 (54%) | 28 (26%) | 10 (9%) | 8 (7%) | 4 (4%) | 108 |

Numbers in each cell indicate the number of subjects exhibiting the symptom and the percent (in parentheses) of observed total symptoms that number represents.
Subjects may have more than one type of symptom during an exposure. Therefore, the total number of symptoms may exceed the number of subjects for a given profile.
* Skin manifestations include symptoms generally classified as peripheral nervous system symptoms: pins and needles, tingling, prickling, urticaria, cutis marmorata (mottling), hot and cold sensations, and edema. Erythema (red rash, not raised) and pruritus (itch) are included under skin manifestations.
† Respiratory symptoms include substernal distress, cough, and dyspnea.
‡ Central nervous system symptoms include headache, dermatomal skin symptoms, dizziness, fatigue, and light-headedness.
§ Other symptoms include muscle pain and pain not perceived in joint or muscle.

(where resolution of a symptom may not be immediately possible), the more participants that develop DCS early in an exposure, the larger the number that may progress to serious events which could impact the outcome of the mission and/or the well-being of the participant.

There are potential shortcomings of the data used in this study. One criticism is that our data was a mixture of independent and repeated measures, and that, for the repeated measures, the order of profiles was not balanced. We argue that since only 6 of the 95 control subjects participated in any BiP profile, the most important comparisons (any BiP vs. control) were essentially performed with independent data, thus satisfying the criterion of the statistical tests. There might also be concerns that the control and BiP subjects represent different anthropometric/physiologic populations since, statistically, average body fat was higher and age was lower in the controls. Realistically, the average ages were within about 4-5 yr of each other and were all well within the age range of the active military population. The body fat differences might be of more concern, but, again, the averages all fall within the range of those seen in relatively fit personnel. Also, since the body fat averages are based on smaller sample sizes due to missing data, we are less confident that they are good representations of the population averages. Finally, one may wonder, since there were no women in the control group, what impact the small number of women in the BiP groups had on the results. Webb et al. (14) did not find gender differences with respect to DCS. Furthermore, since the operational groups of interest in this study (e.g., U-2 pilots) are comprised of both genders, we felt that it was important to include the women in our analyses. However, had we eliminated them, we would have found the same significant effects that we have reported in this paper.

This study was designed to cover a wide range of air breaks (10 to 60 min), with one goal being to estimate a "safe" limit for air breaks that would have operational value. We originally hypothesized that breaks of 10 or 20 min during a 1-h PreOx would not increase the risk of DCS compared to no break. Our results disproved this hypothesis. It is very reasonable to assume that a break of just a few breaths (such as might occur if a mask adjustment were necessary) would likely not alter the protection provided by the PreOx. But what is the effect of a 5-min, 3-min, or even 1-min break? The slightly less pronounced effects seen for the 10-min BiP compared to the 20- and 60-min BiPs suggest that a safe limit does exist. A related issue concerns the timing of the air break. In this study, an air break $\geq$10 min occurring at the midpoint of a 1-h PreOx increased the risk of developing DCS during at least the first 2 h of a subsequent 9144-m (30,000-ft) altitude exposure, compared to that same exposure with no air break. Would an earlier air break have had less impact on DCS rates, or a later air break a more profound effect? And, of course, the more complex question: What effect does the length of the air break combined with the time of its occurrence have on the protection provided by PreOx? These questions, and others, remain unanswered.

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